EXHIBIT A

2023-2434

United States Court of Appeals for the Federal Circuit

BAYER PHARMA AKTIENGESELLSCHAFT,

Appellant,

– v. –

MYLAN PHARMACEUTICALS INC.,
TEVA PHARMACEUTICALS USA, INC.,
INVAGEN PHARMACEUTICALS INC.,

Appellees.

On Appeal from the United States Patent and Trademark Office, Patent Trial and Appeal Board, in No. IPR2022-00517 Honorable Ryan Holbrook Flax, Administrative Patent Judge, Honorable Tina E. Hulse, Administrative Patent Judge and Honorable Robert A. Pollock, Administrative Patent Judge

REPLY BRIEF FOR APPELLANT BAYER PHARMA AKTIENGESELLSCHAFT

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MAY 24, 2024

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UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

CERTIFICATE OF INTEREST

Case Number 2023-2434

Short Case Caption Bayer Pharma Aktiengesellschaft v. Mylan Pharms. Inc.

Filing Party/Entity Bayer Pharma Aktiengesellschaft

Instructions:

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I certify the following information and any attached sheets are accurate and complete to the best of my knowledge.

Date: 05/24/2024

Signature: /s/ Dov P. Grossman

Name: Dov P. Grossman

1. Represented Entities. Fed. Cir. R. 47.4(a)(1).	**2. Real Party in Interest.** Fed. Cir. R. 47.4(a)(2).	**3. Parent Corporations and Stockholders.** Fed. Cir. R. 47.4(a)(3).
Provide the full names of all entities represented by undersigned counsel in this case.	Provide the full names of all real parties in interest for the entities. Do not list the real parties if they are the same as the entities. ☐ None/Not Applicable	Provide the full names of all parent corporations for the entities and all publicly held companies that own 10% or more stock in the entities. ☐ None/Not Applicable
Bayer Pharma Aktiengesellschaft	Bayer AG	Bayer AG
	Janssen Pharmaceuticals, Inc. (represented by Sidley Austin LLP, not Williams & Connolly LLP)	Johnson & Johnson (Janssen)
	Bayer Intellectual Property GmbH	Bayer AG
	Bayer U.S. LLC	Bayer AG
	Bayer Medical Care Inc.	Bayer AG
	Bayer HealthCare LLC	Bayer AG

☐ Additional pages attached

4. Legal Representatives. List all law firms, partners, and associates that (a) appeared for the entities in the originating court or agency or (b) are expected to appear in this court for the entities. Do not include those who have already entered an appearance in this court. Fed. Cir. R. 47.4(a)(4).

☐ None/Not Applicable ☐ Additional pages attached

Kathryn S. Kayali	Williams & Connolly LLP	represented Bayer in the IPR
Julie L. Tavares	Williams & Connolly LLP	represented Bayer in the IPR

5. Related Cases. Other than the originating case(s) for this case, are there related or prior cases that meet the criteria under Fed. Cir. R. 47.5(a)?

☑ Yes (file separate notice; see below) ☐ No ☐ N/A (amicus/movant)

If yes, concurrently file a separate Notice of Related Case Information that complies with Fed. Cir. R. 47.5(b). **Please do not duplicate information.** This separate Notice must only be filed with the first Certificate of Interest or, subsequently, if information changes during the pendency of the appeal. Fed. Cir. R. 47.5(b).

6. Organizational Victims and Bankruptcy Cases. Provide any information required under Fed. R. App. P. 26.1(b) (organizational victims in criminal cases) and 26.1(c) (bankruptcy case debtors and trustees). Fed. Cir. R. 47.4(a)(6).

☑ None/Not Applicable ☐ Additional pages attached

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INTRODUCTION

Contrary to Mylan's assertion that "[p]atentability does not, and cannot, turn on clinical results alone," Mylan Br. 42,[1] a method claim based on the results of a clinical trial *can* be patentable when the results were neither disclosed in the prior art nor are obvious. That concept is grounded in *Sanofi v. Watson Laboratories Inc.*, 875 F.3d 636 (Fed. Cir. 2017), which evaluated an efficacy limitation in terms of obviousness precisely because the prior art did not disclose the clinical trial results at issue. *Id.* at 646-650. Thus, rather than attempting to create a *per se* rule that results of a clinical trial are patentable—as Mylan incorrectly argues that Bayer seeks to do, Mylan Br. 42-43—Bayer's point is that the lack of any prior-art results here means that "clinically proven effective" should be judged using the standard for obviousness, as in *Sanofi*. Obviousness is a fact-dependent inquiry, and may well in some instances render unpatentable a claim to a "clinically proven effective" regimen. Here, however, the Board made no such finding. That is not surprising, as the evidence showed that the POSA would not have reasonably expected the COMPASS trial to provide clinical proof of efficacy.

With respect to "clinically proven effective," Mylan's Response fails to justify

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[1] Given that Teva and InvaGen did not present unique evidence or argument, this Reply refers to evidence and arguments presented by Mylan. *See* Opening Br. 5, n.1.

the Board's exceptional decision to read out that limitation from the body of the claims. Emblematic of Mylan's faulty approach is its reliance on a concurrence, not controlling law, to attempt to distinguish caselaw that contradicts its reading of *Bristol-Myers Squibb Co. v. Ben Venue Laboratories, Inc.*, 246 F.3d 1368 (Fed. Cir. 2001) ("*BMS*").

With regard to inherency, not only do Mylan's arguments reinforce that the Board misapplied the legal test, but—tellingly—Mylan points to no evidence that clinical proof of efficacy is inherent to a clinical trial. Nor does Mylan point to any evidence that contradicts the evidence cited in Bayer's Opening Brief that proof of efficacy is *not* inherent to a clinical trial. Opening Br. 42-45.

By the same token, Mylan's contention that "a first product comprising rivaroxaban and aspirin" is not properly on appeal is a transparent attempt to divert attention from its own failure of proof. There is no question that Bayer raised a dispute regarding the construction of that phrase and that the Board decided the issue. Appx0019-Appx0021; Appx0494. If Bayer's construction is correct, then *Mylan* needed to adduce evidence of invalidity based on that construction. It is Mylan's burden to prove invalidity, not Bayer's burden to prove validity. But Mylan failed to provide evidence under Bayer's construction, which is confirmed by the fact that Mylan nowhere identifies such evidence.

For Ground 5, while Mylan suggests that the Board did analyze its proposed

combination of Foley (COMPASS) and Plosker (ATLAS ACS), that position is contradicted by Mylan's concession that "the ATLAS trial" did not have "the least bearing on what the Board actually decided in its final decision." Mylan Br. 5. Mylan goes on to allege that Bayer failed to dispute whether there was a motivation to combine Foley and Plosker with a reasonable expectation of success. That too is wrong. Bayer's Patent Owner Response argued that the Board's Institution Decision "was correct" to reject Mylan's assertion that the POSA "would have combined the clinical efficacy results from Plosker's ATLAS trial for ACS patients with Foley's COMPASS method of treating patients with stable CAD with a reasonable expectation of success." Appx0511. Mylan's forfeiture allegation is thus entirely without basis.

Finally, with respect to objective evidence of nonobviousness, Mylan nowhere identifies any acknowledgment by the Board of Bayer's argument that the POSA would not have expected COMPASS to demonstrate clinical proof of efficacy. Nor does Mylan point to any Board analysis of that issue. Instead, Mylan relies on a discussion of whether the unexpected decision to terminate COMPASS early was a difference in degree rather than a difference in kind. Mylan Br. 58-59. But that does not compensate for the Board's failure to address whether the results of COMPASS themselves constitute an unexpected property. It is not sufficient that the Board analyzed, in its own words, whether the "fact alone" of ending COMPASS

early was an unexpected property. Appx0036.

In sum, the Board's decision regarding Grounds 3-5 should be reversed. To the extent the Court believes there are any remaining issues for the Board to adjudicate, then the Board's decision should be vacated and the case remanded.

ARGUMENT

I. The Board Erred in Holding that "clinically proven effective" Is Non-Limiting

The Board held "clinically proven effective" to be non-limiting based on *BMS*—a narrow exception to the general rule that one cannot ignore limitations in the body of a claim. Appx0013-Appx0019; Opening Br. 33-40. Mylan fails to justify that ruling.

A. Mylan's claim construction-based arguments do not justify reading out "clinically proven effective" from the claims

Mylan initially offers a series of claim construction-based arguments to try to defend the Board's decision. None has merit.

First, Mylan seeks to "collapse" "clinically proven effective" with the numerical doses of rivaroxaban and aspirin by suggesting that the claims somehow "defin[e]" "clinically proven effective" to mean those numerical amounts of rivaroxaban and aspirin. Mylan Br. 23 ("two amount-defining phrases collapse"); *see id.* 1, 9, 22, 42. That is wrong. The body of claim 1 refers to administration of amounts of rivaroxaban and aspirin that are "clinically proven effective." In a

separate, subsequent clause, the claim recites specific numerical doses of rivaroxaban and aspirin. Nothing about that language or structure is definitional, or otherwise treats the two phrases as interchangeable. Rather, the subsequent recitation of numerical doses specifies what clinically proven effective amounts are being administered. The phrase "clinically proven effective" could potentially be satisfied by numerical doses that differ from those recited in the claim. Likewise, the numerical doses of rivaroxaban and aspirin do not, standing alone, indicate that they are clinically proven effective.

The specification reinforces this understanding. Contrary to Mylan's suggestion, *see* Mylan Br. 25-26, the specification does not always use "clinically proven effective" in combination with the claimed numerical doses of rivaroxaban and aspirin. For example, the '310 patent states: "The methods and products of the invention concern dosages that are clinically proven safe and effective," without reference to any numerical amount. Appx0061 (col. 10, ll. 9-10). The patent also identifies numerical amounts of rivaroxaban and aspirin that fall outside the doses specified in the claims. For example, the specification individually lists doses of rivaroxaban between 0.5 mg and 3.5 mg, increasing by 0.1 mg increments, and identifies those values as "[d]osages to be used in embodiments of the present invention." Appx0060 (col. 8, ll. 1-5). Similarly, for aspirin, the specification lists a series of individual doses between 30 mg and 150 mg to be administered "once

daily in combination with twice daily rivaroxaban." Appx0060 (col. 8, ll. 9-16); *see id.* (col. 8, ll. 16-64).

Second, Mylan asserts that "clinically proven effective" is non-limiting because it does not change the "manipulative steps" of the claimed method. *E.g.*, Mylan Br. 37. However, this Court has rejected the proposition that language in a method claim is only limiting if it changes the manipulative steps. *See Griffin v. Bertina*, 285 F.3d 1029, 1033-34 (Fed. Cir. 2002). Instead, the question is not whether the steps are changed, but whether the language constitutes a statement of intended purpose. *See BMS*, 246 F.3d at 1375-76; *see also Griffin*, 285 F.3d at 1033-34. The "wherein" clauses in *Allergan* did not change the manipulative steps, yet those clauses were found limiting because the record showed they were material to patentability. *Allergan Sales, LLC v. Sandoz, Inc.*, 935 F.3d 1370, 1372-76 (Fed. Cir. 2019). The same is true here. Opening Br. 33-35.

Even if Mylan's approach were correct, Mylan is wrong that "clinically proven effective" does not change the steps of the method. *See* Opening Br. 35. Prior to the COMPASS results, administering the numerical amounts of rivaroxaban and aspirin in the claims would not have constituted administering clinically proven effective amounts of rivaroxaban and aspirin. That is what clearly distinguishes the invention from the prior art: proving in a clinical trial that the numerical amounts of rivaroxaban and aspirin are effective for the recited indication in the specified patient

population, despite that never having been done before (novelty), and despite the evidence that the POSA would not reasonably expect COMPASS to successfully provide for such clinical proof of efficacy (nonobviousness). Opening Br. 51-53; *see, e.g.*, Appx5085-Appx5086 (¶¶ 131-141). Again, the Board never found that the POSA would have reasonably expected COMPASS to successfully provide clinical proof of efficacy, but rather based its obviousness holding on its earlier anticipation determination. Appx0028-Appx0031.[2]

Third, Mylan seeks to discount the prosecution history by pointing to the Board's holding that the Supplemental Examination Unit purportedly did not have *BMS* in front of it. Mylan Br. 27. Neither the Board nor Mylan offer any evidence that those three examiners were unaware of the decision. In any event, the Supplemental Examination Unit *did* have the specification and claims, which they interpreted to require clinical proof of efficacy—and found no substantial new question of patentability on that basis. Appx0319 (quoting Appx3541-Appx3542);

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[2] While Mylan in its Petitioner's Reply attempted to respond to Bayer's evidence that the POSA would not have had a reasonable expectation of success, and cites those responses in its Response, Mylan Br. 24, Mylan's allegations were meritless. They mischaracterized the record (Dr. Weitz's purported admission about ATLAS ACS) or relied on non-prior art information that in any event contradicted Mylan's position (whether ATLAS ACS and COMPASS overlapped). *See, e.g.*, Appx2708; Appx2857-Appx2860 (123:24-124:9, 125:23-126:10), Appx4801; Appx4872, Appx4875. It is therefore unsurprising that the Board did not accept Mylan's position.

see Appx5024-Appx5025 (¶ 44). Moreover, the Supplemental Examination Unit's conclusion came after Bayer presented arguments that relied on "clinically proven effective" to distinguish the prior art. Appx3321-Appx3322 ("[b]ecause the claims recite administering rivaroxaban and aspirin in amounts that are *clinically proven effective*, the claims are patentable and not anticipated" (emphasis added)). Mylan thus ignores *Phillips*'s holding that the prosecution history is relevant to claim construction because it "provides evidence of how the PTO and the inventor understood the patent." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1317 (Fed. Cir. 2005) (*en banc*). That prong of *Phillips* formed a critical aspect of the analysis not only in *BMS*, but also in subsequent authority that distinguished the *BMS* exception. *See BMS*, 246 F.3d at 1375-76; *Allergan*, 935 F.3d at 1372-76; *L.A. Biomedical Rsch. Inst. at Harbor-UCLA Med. Ctr. v. Eli Lilly & Co.*, 849 F.3d 1049, 1053-54, 1061 (Fed. Cir. 2017) ("*Eli Lilly*").

Fourth, while Mylan suggests that its expert Dr. Zusman did not treat "clinically proven effective" as limiting, Mylan Br. 28, that mischaracterizes the record. Mylan's sole support is Dr. Zusman's statement that "running a clinical trial to confirm efficacy of a drug regimen does not constitute an invention." Mylan Br. 28 (quoting Appx1308-1309 (¶ 60)). Even in isolation, that excerpt does not demonstrate that Dr. Zusman treated "clinically proven effective" as non-limiting. Mylan also omits the relevant part of his testimony. The complete testimony reads:

"I also understand"—an understanding presumably provided by counsel—"that the efficacy of a particular dosage amount of a drug, or multiple drugs in combination, is inherent to the drugs administered. *That is*—running a clinical trial to confirm efficacy of a drug regimen does not constitute an invention." Appx1308 (¶ 60) (emphasis added). The emphasized language shows that Dr. Zusman was referring to his earlier-stated "understand[ing]" about the law of inherency, not offering an opinion as to what legally qualifies as an invention.

Finally, the case law cited by Mylan nowhere justifies reading "clinically proven effective" out of the claims. For example, while Mylan relies on *Alcon Research, Ltd. v. Apotex Inc.*, 687 F.3d 1362 (Fed. Cir. 2012), Mylan Br. 26, *Alcon* addressed whether claim language directed to mast cell stabilization was *inherent*. 687 F.3d at 1369. Indeed, far from supporting the proposition that one can ignore claim limitations, *Alcon* refers to the mast cell stabilization requirement as a "limitation." *Id.* at 1366, 1367, 1369.

Mylan also relies on *Maxell, Ltd. v. Amperex Technology, Ltd.*, 94 F.4th 1369 (Fed. Cir. 2024), for the unremarkable proposition that claims should be read in context. Mylan Br. 24. Neither that principle, nor its application in *Maxell*—which held that the claim at issue was not indefinite because there was "no contradiction" between two limitations, *id.* at 1373—has any bearing here. Rather, the issue is whether Mylan (and the Board) should be permitted to treat the phrase "clinically

proven effective" as non-limiting, an outcome *Maxell* not once contemplated, much less endorsed.

B. Mylan fails to justify the Board's reliance on *BMS*

Mylan's attempts to prop up the Board's reliance on *BMS* do not pass muster.

Mylan asserts that "clinically proven" does not add to the phrase "effective" because it does not "change[] the amounts of rivaroxaban and aspirin expressly recited in the claims." Mylan Br. 29-30 (quoting Appx0017). That ignores the salient issue. *BMS* held: "The express dosage amounts are material claim limitations; *the statement of the intended result* of administering those amounts does not change those amounts *or otherwise limit the claim*." 246 F.3d at 1375. Thus, the question is not whether "clinically proven effective" itself changes the numerical doses of rivaroxaban and aspirin recited in the claim, but whether that language constitutes "the intended result" of the method or "otherwise limit[s] the claim." *Id.* In that regard, and as discussed in Bayer's Opening Brief, "clinically proven effective" is *not* an intended result of practicing the claimed methods. Opening Br. 33-35. And "clinically proven effective" *is* a material limitation that *does* limit the claim—as recognized by, for example, the Supplemental Examination Unit. *Supra*, § I.A. That distinguishes the role of the claim language here from the unsolicited applicant amendment made after allowance in *BMS*. *See* 246 F.3d at 1375; *Allergan*, 935 F.3d at 1376; *see also In re Copaxone Consol. Cases*, 906 F.3d 1013, 1023-24

(Fed. Cir. 2018) (this Court was "unpersuaded" that the added claim language "was necessary or relevant to the examiner's approval").

Mylan nevertheless asserts that "clinically proven effective" is an expression of intended result because "[t]he intent expressed in the phrase 'clinically proven effective' is that the amounts actually possess the ***property*** of being clinically effective." Mylan Br. 30; *see id.* 1. The argument is yet another example of Mylan reading out claim language ("proven"). It also wrongly conflates the doctrine of inherency with an expression of an intended result. Whether (a) something is an inherent property that would necessarily satisfy a claim limitation is a distinct inquiry from whether (b) the claim language needs to be satisfied in the first instance or can be read out of the claim.

C. Mylan fails to distinguish cases that limit *BMS*

Mylan not only fails to show that *BMS* is applicable, but its treatment of the case law cited in Bayer's Opening Brief reinforces that *BMS* is a narrow exception.

Regarding *Allergan*, Mylan's sole response is to quote from the concurrence. Mylan Br. 35. A concurring opinion is not the law. *Ministerio Roca Solida v. United States*, 778 F.3d 1351, 1355 (Fed. Cir. 2015). "It goes without saying that the majority opinion, not the gloss that the concurrence seeks to place thereon, is controlling." *Dababnah v. Keller-Burnside*, 208 F.3d 467, 471 n.3 (4th Cir. 2000). In any event, the concurrence in *Allergan* does not even characterize the majority's

opinion. Instead, it offers an alternate explanation as to why the concurring Judge "would arrive at that conclusion *by following a slightly different path*." *Allergan*, 935 F.3d at 1377 (Prost, C.J., concurring) (emphasis added).

As for *Eli Lilly*, Mylan argues that this Court distinguished cases like *BMS*—and purportedly like this one—"in which the claims contain express dosage amounts as material claim limitations, *and* in which efficacy is 'inherent in carrying out the claim steps.'" Mylan Br. 36 (quoting 849 F.3d at 1061) (emphasis modified). While Mylan focuses on the phrase "express dosage amounts as material claim limitations," Mylan Br. 36, Mylan ignores the "and" in the very same sentence that links the language concerning dosage amounts to the concept of "inherency." Mylan cannot credibly suggest that merely whether a claim contains "dosage amounts as material claim limitations" grants license to ignore other claim language, especially where the other language was deemed material to patentability by the PTO. And Mylan nowhere addresses the other points raised in Bayer's Opening Brief concerning why this case is akin to *Eli Lilly* and distinct from *BMS*, including that "clinically proven effective" demands efficacy (that is proven in a clinical trial) whereas the claims in *BMS* did not. Opening Br. 38-39; *Eli Lilly*, 849 F.3d at 1061.

Finally, Mylan argues that *Copaxone* is similar to the present case, analogizing *Copaxone*'s claim language "sufficient to alleviate the symptom" to "clinically proven effective." Mylan Br. 36-37. That is yet another example of

Mylan improperly reading out "clinically proven" from the claims. Even if "sufficient to alleviate the symptoms" may be read as a statement of intended effect, "clinically proven effective" requires proof from a clinical trial. Opening Br. 27-28, 33-34. Moreover, in *Copaxone*, as in *BMS*, the claim language was not necessary to the examiner's approval, an important contrast to the facts here. *Copaxone*, 906 F.3d at 1023-24; *BMS*, 246 F.3d at 1375; *see Allergan*, 935 F.3d at 1376 (distinguishing *Copaxone* and *BMS* on the basis that the disputed clauses were "material to the Examiner's patentability determination").

II. The Board Erred in Holding that "clinically proven effective" Is Inherent

Bayer's Opening Brief demonstrated that the Board's inherency findings should be reversed, as (1) the Board misapplied the test for inherency with respect to Foley's disclosure, and (2) the uncontroverted evidence from both sides' experts was that it is *not* inherent that a clinical trial will provide clinical proof of efficacy. Opening Br. 40-45. Mylan does not justify the Board's misapplication of the test for inherency. Nor does Mylan point to any evidence supporting its position that a clinical trial will inherently provide clinical proof of efficacy. That warrants reversal.

First, Mylan asserts that Bayer "misunderstand[s]" the legal test for inherency, contending that the purpose of COMPASS was to confirm "the expected property of clinical efficacy." Mylan Br. 38. But the Board never found that the

results of COMPASS were "expected," and the record does not support Mylan's allegations as to the purpose of COMPASS. In any event, Mylan's description of inherency misses the mark. To be inherent, the issue is not whether a property is "expected." Nor is the "purpose of COMPASS" a relevant consideration. Rather, to be inherent, a result must be "inevitabl[e]" or the missing limitation must be "necessarily present." *In re Montgomery*, 677 F.3d 1375, 1379-80 (Fed. Cir. 2012); *Schering Corp. v. Geneva Pharms., Inc.*, 339 F.3d 1373, 1377-78 (Fed. Cir. 2003).

On that measure, the Board's analysis was legally erroneous. The Board concluded that "clinically proven effective" was inherent "because the claimed process was confirmed by the *same* COMPASS study disclosed by Foley." Appx0026. Again, however, the question is not whether an experiment disclosed in the prior art happened to produce the result at issue, but whether it was *inevitable* that it would do so. Inherency "may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient." *Bettcher Indus., Inc. v. Bunzl USA, Inc.*, 661 F.3d 629, 639 (Fed. Cir. 2011). In that regard, Foley disclosed a clinical trial with nearly 6000 fewer patients than the COMPASS trial disclosed in the '310 patent. *Compare* Appx2352 *with* Appx0064 (col. 15, ll. 25-29). Yet Mylan points to no evidence that Foley's disclosure would inevitably or necessarily result in clinical proof of efficacy—or even that it would provide clinical proof of efficacy at all. That alone

shows error in the Board's decision.

Similarly, Mylan points to no evidence that a clinical trial will inherently provide clinical proof of efficacy, let alone evidence that would contradict the uniform testimony of both side's experts that such a result is *not* inherent. Appx5093-Appx5094 (¶ 151), Appx4309-Appx4313, Appx4350-Appx4352 (42:8-44:8), Appx4353 (45:4-13). That further undermines the Board's decision.

Second, and in apparent recognition that there is no evidence to support inherency, Mylan cites *Montgomery* for the proposition that the existence of a clinical trial can support a finding of inherency. Mylan Br. 38-39. That is yet another example of Mylan reading "clinically proven effective" out of the claims. In *Montgomery*, the claims were directed to a method "for the treatment or prevention of stroke or its recurrence." 677 F.3d at 1377. In deciding the appeal, this Court expressed skepticism that the claims required efficacy given the absence of claim language to that effect. *Id.* at 1380. The Court nevertheless held that assuming, *arguendo*, the claims did require efficacy, any such limitation was inherently anticipated in carrying out the method steps, because "treating stroke-prone patients with [the drug] does in fact inevitably treat or prevent stroke," a point that Montgomery apparently did "not dispute." *Id.* at 1381. That analysis is inapposite. There is no evidence here that administering rivaroxaban and aspirin to a patient "inevitably" provides the clinical proof of efficacy required by the claims—

indeed, the evidence is to the contrary. Nor does the analysis in *Montgomery* address the salient claim language, which requires not mere efficacy, but *clinical proof* of efficacy.

Third, Mylan tries to distinguish *Sanofi* by arguing that inherency was not at issue in that case. That is precisely the point. If proof of efficacy were inherent from a clinical trial, then it *would* have been at issue in *Sanofi*, and this Court's holding—affirming that the disclosure of a clinical trial protocol did not render obvious the claimed efficacy limitation—would be incorrect. Opening Br. 45. The better conclusion is that, consistent with the analysis in *Sanofi* and the uncontroverted evidence here, it is *not* inherent that a clinical trial will provide clinical proof of efficacy.

Fourth, Mylan attempts to distinguish *Endo Pharmaceuticals Solutions, Inc. v. Custopharm Inc.*, 894 F.3d 1374 (Fed. Cir. 2018), on the basis that "the actual formulation of the composition [used in the prior art clinical trial] was not reported until after the patent's priority date." Mylan Br. 40. Exactly. *Endo* reinforces that the inherency analysis must remain centered on what the prior art *reference* discloses to the POSA. *See Endo*, 894 F.3d at 1383 ("[T]he incomplete description of the TU injection composition elements [in the prior art reference] denied skilled artisans from having access to that composition, thereby precluding use of the inherency doctrine to fill in disclosure about the product missing from the Articles."). Mylan

did not attempt to adduce evidence that COMPASS as disclosed in Foley would have established clinical proof of efficacy.

Fifth, citing the Board's decision and *King Pharmaceuticals, Inc. v. Eon Labs, Inc.*, 616 F.3d 1267, 1279 (Fed. Cir. 2010), Mylan asserts that "[t]he question is not whether clinical trials may exist where the disclosed dosing regimen may not be clinically proven effective," because that "would be akin to concluding a property cannot be inherent to a disclosed prior-art process because it is possible to have a poorly designed experiment fail to detect the property," Mylan Br. 39 (quoting Appx0026). The argument assumes that a properly designed clinical trial would inherently provide clinical proof of efficacy, when the uncontroverted expert evidence refutes that assumption. Opening Br. 42-43. Moreover, Mylan misses the point. The Board concluded that clinical proof of efficacy was inherent because COMPASS as disclosed in Foley provided clinical proof of efficacy, but that is demonstrably incorrect.

Nor do the facts of *King* support Mylan. *King* found that language directed to "informing the patient" of the efficacy of the regimen—which was known—did not render the claim novel. 616 F.3d at 1278. That is a far cry from the present situation, where a multi-year, worldwide, clinical trial involving over 27,000 patients was performed in an attempt to see if clinical proof of efficacy could be shown in the first instance. Appx0063-Appx0064 (col. 13, ll. 36 to col. 15, ll. 63); Appx3611-

Appx3622.

Finally, Mylan alleges that Bayer seeks a rule that clinical trial results are *per se* patentable. Mylan Br. 42-43. That is wrong. The fact that clinical proof of efficacy is not inherent to COMPASS does not mean that all clinical trial results are patentable. There will almost certainly be clinical trials where there is a reasonable expectation of successfully proving clinical efficacy, a fact that would negate patentability. Here, however, the Board made no such finding.

III. Mylan Adduced No Evidence that Claims 5-8 Are Invalid Under the Correct Construction

As discussed in Bayer's Opening Brief, the phrase "a first product *comprising* rivaroxaban *and* aspirin" in claims 5-8 refers to a single dosage form that contains *both* rivaroxaban *and* aspirin. Opening Br. 46-48. Mylan seeks to avoid the merits of that issue by arguing that Bayer's construction was "moot" and "forfeited." Mylan Br. 47-48 (citing Appx0022). Mylan's position is based on the incorrect notion that, to preserve its argument, Bayer needed to demonstrate the nonobviousness of claims 5-8 under that alternative construction. That misperceives the burden of proof. "[T]he burden of proving invalidity in an IPR remains on the *petitioner* throughout the proceeding." *Fanduel, Inc. v. Interactive Games LLC*, 966 F.3d 1334, 1341 (Fed. Cir. 2020) (emphasis added). "[I]t is inappropriate to shift the burden to the patentee after institution to prove that the patent is patentable." *In re Magnum Oil Tools Int'l, Ltd.*, 829 F.3d 1364, 1375 (Fed. Cir. 2016). In its

Petition, Mylan proposed the construction adopted by the Board, *i.e.*, that reads "a first product comprising rivaroxaban and aspirin" out of the claim and merely requires the two drugs to be administered around the same time. Appx0092-Appx0093. The Board adopted that construction in the Institution Decision. Appx0306-Appx0308. Bayer disputed that construction and preserved the objection by advocating for its alternative construction in the Patent Owner's Response. Appx0494; Appx0509-Appx0510; Appx5063-Appx5065 (¶¶ 103-105); Appx5102-Appx5103 (¶¶ 163-164). Thus, it was *Mylan's* obligation in its Petitioner Reply to show why claims 5-8 were obvious under Bayer's proposed construction, as there was a risk that Bayer's construction was correct. Mylan failed to do so. That is highlighted by the fact that Mylan does not identify any evidence it proffered to the Board that claims 5-8 are obvious under Bayer's construction. That requires reversal.

Indeed, Mylan's arguments undermine its attempt to shift the burden of proof to Bayer. The Petition alleged that the claims were unpatentable because Mylan understood "a first product" to include simultaneous or near-simultaneous administration of different dosage forms. Appx0092-Appx0093; Appx0145-Appx0147. Given the clear language of claims 5-8, Mylan's actions reflect that it perceived some shortcoming in the prior art, and thus pursued claim construction as the strategy to overcome that evidentiary deficiency. That understanding is

reinforced by the fact that, after Bayer submitted its Patent Owner Response and highlighted the problems with Mylan's construction, Mylan rejected the opportunity to present argument or evidence under Bayer's construction. Instead, Mylan doubled down on the incorrect construction in its Petition. Appx0631-Appx0632. Mylan's current attempts to circumvent Bayer's construction as either moot or forfeited only underscore that Mylan did not adduce any evidence of obviousness under that construction.

Tacitly acknowledging this failure of proof, Mylan suggests that, as a matter of law, "little is more obvious than combining two things previously used together into a single form." Mylan Br. 47. That is a new argument on appeal that is entitled to no weight. *See Golden Bridge Tech., Inc. v. Nokia, Inc.*, 527 F.3d 1318, 1322 (Fed. Cir. 2008). Moreover, there is no such legal principle. The mere fact that there are cases in which it was obvious to combine "two things" into "a single form" does not mean it would be obvious to do so in every circumstance as a matter of law. *See Sanofi-Aventis Deutschland GmbH v. Glenmark Pharms. Inc., USA*, 748 F.3d 1354, 1361 (Fed. Cir. 2014) (combining two known drugs in a single dosage form was nonobvious); *Pozen Inc. v. Par Pharm., Inc.*, 696 F.3d 1151, 1165 (Fed. Cir. 2012) (similar); *see also Allergan*, 935 F.3d at 1375-76 (upholding patentee's reliance on the unexpected efficacy and safety of a formulation combining two known drugs to distinguish the claimed methods from the prior art).

Mylan tries to save its challenge by asserting that the "product" can be "a kit or blister pack," an argument not presented in its Petition. Mylan Br. 44; *see id.* 14 (citing Appx0021). The Board's construction did not so limit the claim language. Appx0021. In any event, Mylan incorrectly interprets the claim. The '310 patent treats "product" as referencing a dosage form. *E.g.*, Appx0062 (col. 12, ll. 43-48; col. 12, ll. 54-56) ("The pharmaceutical product may also contain pharmaceutically suitable excipients, such as fillers, disintegrants, etc."); *see also* Appx0060-0061 (col. 8, l. 65 to col. 9, l. 2) ("A combination dosage form further comprises a pharmaceutically acceptable excipient."). The '310 patent also treats "packs" and "kits" as distinct from dosage forms that contain all of the components. Appx0061 (col. 9, ll. 9-18); *see* Appx5064-Appx5065 (¶ 105).

Even if one were to somehow credit Mylan's "kit" or "blister pack" argument, Mylan adduced no evidence as to how such a kit or blister pack would be obvious over Foley or Plosker. That is not surprising, as Mylan's hypothetical "kit" or "blister pack" would contain all three doses—two of rivaroxaban and one of aspirin—in a single "product." *See* Appx4391-Appx4392 (83:2-84:8) (Zusman deposition testimony referring to a "card" with one capsule containing two substances and one capsule containing a single substance); Appx5064-Appx5065 (¶ 105). The "kit" or "blister pack" thus could not satisfy the claim 5 requirements for two products, *i.e.*, a "first product comprising rivaroxaban and aspirin" *and* a

"second product comprising rivaroxaban."

IV. The Board Failed to Perform a Proper Obviousness Analysis for Ground 5

Bayer's Opening Brief identified a further flaw in the Board's Decision—Ground 5 requires the combination of Foley and Plosker, yet the Board failed to explain why the POSA would have had reason to combine those references with a reasonable expectation of success. Opening Br. 55-58. In response, Mylan does not point to anywhere in the Board's decision where it performed such an analysis. To the contrary, Mylan affirmatively acknowledges that ATLAS ACS—the trial discussed in Plosker—had nothing to do with the Board's decision. Mylan Br. 5. That is yet another reason for, at a minimum, vacatur and remand.

A. Bayer did not forfeit the argument that the Board failed to perform a proper obviousness analysis for Ground 5

Mylan accuses Bayer of raising its argument "regarding the Board's obviousness determination" of claims 3-4 and 6-7 "[f]or the first time on appeal." Mylan Br. 54. It is unclear when Mylan expects Bayer to have earlier raised the argument. Bayer cannot divine the Board's intentions before it issues a decision, nor is that what the law requires. *Cf. Hawknet, Ltd. v. Overseas Shipping Agencies*, 590 F.3d 87, 92 (2d Cir. 2009) ("[T]he doctrine of waiver demands conscientiousness, not clairvoyance, from parties.").

Even supposing Mylan meant to refer to its own obviousness challenge,

Mylan's arguments do not hold water. In its Patent Owner Response, Bayer quoted from the Institution Decision: "We are also not persuaded, on this record, that Petitioner has shown sufficiently that a person of ordinary skill in the art would have combined the clinical efficacy results from Plosker's ATLAS trial for ACS patients with Foley's COMPASS method of treating patients with stable CAD with a reasonable expectation of success." Appx0511. Bayer then stated: "*The Board's analysis was correct*." *Id.* (emphasis added). Bayer also referenced earlier portions of its Response, vast swaths of which addressed, *inter alia*, the differences between ATLAS ACS (discussed in Plosker) and COMPASS (discussed in Foley). *Id.*; *see, e.g.*, Appx0470-Appx0471, Appx0498.

Mylan's citation to *Arendi SARL v. Google LLC*, 882 F.3d 1132, 1137 (Fed. Cir. 2018), does not support its position. The Board in that proceeding addressed the arguments raised by the Patent Owner, which is not the case here. *Google Inc. v. Arendi SARL*, No. IPR2014-00452, 2015 WL 4976582, at *23 (PTAB Aug. 18, 2015) ("*Aside from the above-discussed arguments*. . . Patent Owner does not address separately Petitioners' challenge of [the remaining] claims.") (emphasis added). Indeed, this Court has vacated Board decisions that failed to address arguments advanced by the parties. *See Power Integrations, Inc. v. Lee*, 797 F.3d 1318, 1324-25 (Fed. Cir. 2015).

B. Mylan fails to justify the Board's error

Mylan nevertheless contends that the Board somehow did perform a proper obviousness analysis. The position is meritless.

The Petition alleged that (1) "Foley teaches co-administering twice-daily 2.5 mg rivaroxaban with once-daily 100 mg aspirin to patients with CAD or PAD," and (2) "[f]rom the teachings of Plosker, a POSA would have understood that co-administering twice-daily 2.5 mg rivaroxaban along with a daily dose of 75-100 mg aspirin would have been effective at reducing the risk of myocardial infarction, stroke, or cardiovascular death." Appx0149. While Mylan also relied on the '310 patent's detailed statement of the invention for allegations regarding 75 and 81 mg strengths of aspirin, Mylan only did so in connection with its arguments regarding the combination of Foley and Plosker. Appx0149-Appx0150. Put differently, one first needed to accept that the POSA would combine Foley and Plosker with a reasonable expectation of success before considering those other aspirin doses.

The Institution Decision correctly recognized that Mylan's unpatentability arguments for Ground 5 required proof that the POSA "would have combined the clinical efficacy results from Plosker's ATLAS trial for ACS patients with Foley's COMPASS method of treating patients with stable CAD with a reasonable expectation of success." Appx0319. The Board found that Mylan had not established such proof at the institution stage. *Id.*

In the Final Written Decision, however, the Board abandoned its earlier analytical framework. *Compare* Appx0032-Appx034 *with* Appx0319. That shift further supports the notion that the Board did not perform the required obviousness analysis. Mylan highlights that failure, asserting that "[w]hile Bayer extensively briefs the ATLAS trial [(discussed in Plosker)] and resulting European Medicines Agency (EMA) approval of the claimed method, as well as related questions about stable versus unstable disease—*none of this has the least bearing on what the Board actually decided in its final decision*." Mylan Br. 5 (internal citations omitted) (emphasis added).

Despite that admission, Mylan makes the bare assertion that the Board "addressed Mylan's unrebutted argument and evidence." Mylan Br. 55 (citing Appx0032-Appx0034). Yet the Board made no such finding. As Mylan acknowledges, the Board relied on the detailed statement of the '310 patent invention to observe that the doses of aspirin required by the claims were known in the literature and commercially available. Mylan Br. 55. That does not constitute a finding that the POSA would have had a motivation to combine Foley and Plosker with a reasonable expectation of success. Nor, as noted above, did Mylan ever separately argue (a) any points about the 75 and 81 mg dosages of aspirin from (b) its contention that the Ground 5 claims were obvious based on a combination of Foley and Plosker. Appx0149-Appx0150. And the Board's finding that Plosker is

"consistent" with those aspirin doses (Appx0034) fails to address why the POSA would even look to Plosker when starting with Foley, given that the two references discuss different clinical trials directed to different patient populations. *E.g.*, Appx0058 (col. 3, ll. 12-39); Appx5022-Appx5024 (¶¶ 42-43).

Mylan also contends that because the Board found "clinically proven effective" to be non-limiting and inherent, "the Board did not need to decide whether a POSA would have 'combined the clinical results' from Plosker and Foley," citing *Axonics, Inc. v. Medtronic, Inc.*, 73 F.4th 950, 956-58 (Fed. Cir. 2023). Mylan Br. 56. The argument does not make sense. Ground 5 posits that the POSA would in fact need to combine Foley and Plosker to arrive at the claim limitations in claims 3-4 and 6-7 with a reasonable expectation of success. And nowhere did the Board indicate that it was somehow unnecessary to address that issue because it held that "clinically proven effective" was non-limiting and inherent.[3]

V. The Board's Analysis of Objective Evidence of Nonobviousness Was Flawed

Bayer proffered two categories of objective evidence: (1) the clinical proof of efficacy demonstrated by COMPASS was an unexpected property; and (2) the early

[3] Mylan points to a footnote in the Board's Decision that the 75 mg and 81 mg strengths of aspirin were not tested in COMPASS, and then suggests that it undermines Bayer's position. Mylan Br. 26. That argument constitutes a baseless challenge under 35 U.S.C. § 112 that was neither properly before the Board nor is properly before this Court.

termination of COMPASS was an unexpected property. Appx0512-Appx0515. The Board never analyzed the first category. That is highlighted by Mylan's Response, which quotes the Board's statement that it was "not persuaded that *that fact alone* [*i.e.*, ending COMPASS early] was an unexpected result that is probative of nonobviousness." Mylan Br. 18 (quoting Appx0036) (emphasis added).

Mylan tries to argue otherwise, citing to the Board's quotation of *UCB, Inc. v. Actavis Labs. UT, Inc.*, 65 F.4th 679 (Fed. Cir. 2023), in connection with the Board's finding that COMPASS's "unexpectedly rapid results" did not "necessarily amount to a difference in kind." Mylan Br. 58. That does not support Mylan's position. The Board's decision to quote *UCB* does not show that the Board ever acknowledged Bayer's argument that the clinical proof of efficacy from COMPASS was unexpected, let alone that the Board made a finding that those results were expected or engaged in any analysis as to whether those results were expected. *See* Appx0037. For example, nowhere did the Board discuss how or why the POSA would have expected success from COMPASS, particularly in light of the contrary evidence provided by Bayer. Nor did the Board address other relevant information proffered by Bayer, such as what constituted the closest prior art or literature reflecting unexpected properties. *See* Opening Br. 58-61; *e.g.*, Appx0512-Appx0514; Appx4804-Appx4805; Appx5106-Appx5108 (¶¶ 169-171).

Mylan nevertheless contends that the efficacy results from COMPASS were

expected, claiming that the COMPASS regimen was already "shown to be safe and effective" in ATLAS. Mylan Br. 59. Yet Mylan admits that the Board's decision had nothing to do with ATLAS ACS. *Id.* at 5. Mylan is also wrong. ATLAS ACS was directed to a different group of patients than COMPASS, a fact well-supported by the record, including the '310 patent itself. Appx0058 (col. 3, ll. 12-39) (distinguishing between ATLAS ACS and COMPASS). Moreover, Mylan's argument is inconsistent with its plea that this Court steer clear of addressing issues related to ATLAS ACS because it purportedly "could work mischief in the numerous related cases or on remand." Mylan Br. 5.

VI. Multiple Prejudicial Errors Warrant Reversal, or at a Minimum, Vactur and Remand

Given that "clinically proven effective" is limiting and not inherently anticipated, the Board's anticipation finding for claims 1-2 (Ground 3, anticipation by Foley) should be reversed.

Similarly, the Board's obviousness findings for claims 5-8 should be reversed because Bayer's proposed claim construction of "a first product comprising rivaroxaban and aspirin" is correct, and Mylan never adduced any evidence under that construction. There is no reason to vacate and remand for those claims, since there is no evidence on which the Board could reach a different conclusion under the correct construction.

As for the the Board's obviousness findings for claims 1, 2, 5, and 8 (Ground

4, obviousness over Foley), those were likewise premised on the Board's flawed determination that "clinically proven effective" is non-limiting and inherent. Claims 5 and 8 also suffer from the aforementioned claim construction issue with respect to "first product."

As for Ground 5, (obviousness over Foley and Plosker) the Board's obviousness findings for claims 3-4 were premised on "clinically proven effective" being non-limiting or inherent. The findings for claims 6-7 suffer from the same flaw, in addition to a further deficiency arising from Mylan's failure to adduce any evidence of obviousness under the correct construction of "first product."

Finally, the Board failed to conduct the required obviousness analysis for Ground 5, and likewise failed to analyze all of Bayer's evidence of nonobviousness. To the extent vacatur and remand, rather than reversal, is warranted for any of Grounds 3-5, those flaws further reinforce the case for vacatur and remand.

CONCLUSION

Bayer respectfully requests that the Court reverse the Board's determination that claims 1-8 are unpatentable. Alternatively, Bayer respectfully requests vacatur and remand. In addition, given that Mylan requests that the Board adjudicate Ground 1-2, remand for consideration of those issues can be appropriate.

Respectfully submitted,

MAY 24, 2024

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CERTIFICATE OF COMPLIANCE

1. This brief complies with the type-volume limitation of Fed. R. App. P. 32(a)(7)(B) and Federal Circuit Rule 32(b). This brief contains 6,819 words, excluding the parts of the brief exempted by Federal Rule of Appellate Procedure 32(f) and Federal Circuit Rule 32(b).

2. This brief complies with the typeface requirements of Federal Rule of Appellate Procedure 32(a)(5) and the type style requirements of Federal Rule of Appellate Procedure 32(a)(6). This brief has been prepared in a proportionally-spaced typeface using Microsoft Word in fourteen-point Times New Roman style.

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